Remarks

This Amendment is responsive to the Office Action dated December 17, 2003 (Paper No. 1203) (herein referred to as "Office Action"). Entry of this amendment and reconsideration in view thereof are respectfully requested.

I. Claim Status

Claims 6-9, 12-15 and 30-37 were pending in the application and these claims stood rejected. Claims 6, 12, 30 and 34 have been amended to clarify the invention. Support for the term "humans" can be found, for example, at page 7, lines 4-5. Support for the recitation "suppressing Cox-2 gene expression" can be found, for example, at page 5, lines 22-23. No new matter is added.

II. Response to Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 6-9 and 12-15 under 35 U.S.C. § 112, first paragraph, based on the assertion that the claim being broader than the enabling scope of the disclosure in the application as filed. The Examiner contends that while the specification is enabling only for an *in vitro* method of inhibiting the growth of cancer cells *in vitro* or in mice by administering an effective dose amount of a composition comprising a mixture of theaflavin-3-gallate and theaflavin-3'-gallate, it does not reasonably provide enablement for a method of treating any and all diseases or conditions in any and all animals by modulating Cox-2 gene expression comprising administering to any and all animals the claim designated composition.

Without conceding the validity of this rejection and solely to expedite the prosecution of this application, Applicant has elected to limit claims to humans. To the extent the Examiner maintains that the pending claims, as amended, are not enabled, Applicant respectfully disagrees and maintains its arguments against the rejection presented in the amendment filed with Office on September 25, 2003.

Accordingly, Applicant respectfully submits that the specification does provide sufficient disclosure to enable those skilled in the art to practice the full scope of the claims without undue experimentation. Reconsideration and withdrawal of this rejection are respectfully requested.

Remarks

This Amendment is responsive to the Office Action dated December 17, 2003 (Paper No. 1203) (herein referred to as "Office Action"). Entry of this amendment and reconsideration in view thereof are respectfully requested.

I. Claim Status

Claims 6-9, 12-15 and 30-37 were pending in the application and these claims stood rejected. Claims 6, 12, 30 and 34 have been amended to clarify the invention. Support for the term "humans" can be found, for example, at page 7, lines 4-5. Support for the recitation "suppressing Cox-2 gene expression" can be found, for example, at page 5, lines 22-23. No new matter is added.

II. Response to Rejections Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 6-9 and 12-15 under 35 U.S.C. § 112, first paragraph, based on the assertion that the claim being broader than the enabling scope of the disclosure in the application as filed. The Examiner contends that while the specification is enabling only for an *in vitro* method of inhibiting the growth of cancer cells *in vitro* or in mice by administering an effective dose amount of a composition comprising a mixture of theaflavin-3-gallate and theaflavin-3'-gallate, it does not reasonably provide enablement for a method of treating any and all diseases or conditions in any and all animals by modulating Cox-2 gene expression comprising administering to any and all animals the claim designated composition.

Without conceding the validity of this rejection and solely to expedite the prosecution of this application, Applicant has elected to limit claims to humans. To the extent the Examiner maintains that the pending claims, as amended, are not enabled, Applicant respectfully disagrees and maintains its arguments against the rejection presented in the amendment filed with Office on September 25, 2003.

Accordingly, Applicant respectfully submits that the specification does provide sufficient disclosure to enable those skilled in the art to practice the full scope of the claims without undue experimentation. Reconsideration and withdrawal of this rejection are respectfully requested.

III. Response to Rejections Under 35 U.S.C. §102

Claims 6-8 and 12-14 stood rejected under 35 U.S.C. §102(a) as anticipated by Yang et al., Phytochemicals and Phytopharmaceuticals, (2000), Editors Shahidi et al., AOCS Press, Champaign, Illinois, Chapter 17, pp 192-201 ("Yang" or "Yang et al. (U)"). Applicant respectfully traverses this rejection.

Yang teaches the use of black tea preparations for controlling lung tumors and the NNK-induced hyperproliferation of cells. Yang's preparations contain theaflavins (i.e., theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate and theaflavin-3, 3'-digallate) EGCG, EGC, ECG and EC.

The Examiner admits on page 10 of the Office Action that Yang does not expressly teach the claimed method but maintains that "the claimed functional effect to modulate Cox-2 gene expression is inherent to the method of administering the composition taught by Yang because cancer is associated with Cox-2 gene expression." This contention is unwarranted for at least the following reasons:

1. The claims require suppression of Cox-2 gene expression and there is no evidence that suppression of Cox-2 gene expression is the "natural result flowing from" the use of the black tea preparations taught by the Yang reference.

2. At the most one may speculate that suppression of Cox-2 gene expression may be inherent result of administering the theaflavin preparations taught by Yang. But inherent anticipation requires that the missing descriptive material is "necessarily present," not merely probably or possibly present in the Yang reference.

3. The claims also require an amount of theaflavin-3-gallate and theaflavin-3'-gallate (i.e., TF-2) effective to suppress Cox-2 gene expression. For example, Examples 5 and 6 (at pages 11-13) describe methodology used to demonstrate suppression of Cox-2 gene expression. Specification, for example, at page 5 line 21 through page 6, line 34 teaches that "TF-2 significantly suppressed Cox-2 gene expression in Caco-2 cells. Effects were seen at doses of 50 to 100 μM TF-2 [i.e, theaflavin-3-gallate and theaflavin-3'-gallate mixture] . . . effects of TF-2 were Cox-2-specific." Applicant notes that Yang teaches , at page 196, a black

tea preparation containing theaflavins, which is a mixture of theaflavin (21%), theaflavin-3-gallate (30%), theaflavin-3'-gallate (15%) and theaflavin-3,3'-digallate (28%). It may or may not contain TF-2 sufficient to suppress Cox-2 gene expression. Further uncertainties become evident when one considers the total of various theaflavins (94%) in the mixture disclosed by Yang. The Examiner has not established that TF-2 in an amount effective to suppress Cox-2 gene expression is necessarily present in the preparation taught by Yang.

4. To the extent Yang teaches a method of treating cancer by administering a composition comprising "the same ingredients," Applicant respectfully submits that treating cancer by using the same ingredients is not sufficient for Yang to anticipate the present claims since that teaching does not necessarily mean suppressing Cox-2 gene expression by using an effective amount of TF2. Further, as the Examiner acknowledged on page 11 of the Office Action, that cancer [treatment] "does not necessarily have to be associated with [suppression of] Cox-2 gene expression."

Therefore, the claim limitations "suppressing Cox-2 gene expression" and "theaflavin-3-gallate and theaflavin-3'-gallate mixture . . . in an effective amount to suppress the Cox-2 gene expression" are not inherent to the method of administering the composition taught by Yang and are not met.

As such, given the strict identity required of the test for novelty, the Examiner has not established a *prima facie* case of anticipation in support of the rejection of claims 6-8 and 12-14 based on the Yang reference. Therefore, contrary to the Examiner's assertion, Yang does not anticipate claims 6-8 and 12-14 as it does not teach or disclose each and every limitation in each of these claims.

DE19627344

Claims 6-8, 12-14, 30-32 and 34-36 further stood rejected under 35 U.S.C. §102(b) as anticipated by DE19627344. Applicant respectfully traverses this rejection.

Again, with respect to DE19627344, the Examiner admits on page 13 of the Office Action that Yang does not expressly teach the claimed method but maintains that "the claimed functional effect to modulate Cox-2 gene expression is inherent to the method of administering

the composition taught by DE19627344 because cancer is associated with Cox-2 gene expression." This contention is unwarranted for at least the following reasons:

1. The claims require suppression of Cox-2 gene expression and there is no evidence that suppression of Cox-2 gene expression is the "natural result flowing from" the use of the tea preparations taught by DE19627344 reference.

2. At the most one may speculate that suppression of Cox-2 gene expression may be inherent result of administering the theaflavin preparations taught by DE19627344. But inherent anticipation requires that the missing descriptive material is "necessarily present," not merely probably or possibly present in the DE19627344 reference.

3. The claims also require an amount of theaflavin-3-gallate and theaflavin-3'-gallate (i.e., TF-2) effective to suppress Cox-2 gene expression. For example, Examples 5 and 6 (at pages 11-13) describe methodology used to demonstrate suppression of Cox-2 gene expression. Specification, for example, at page 5 line 21 through page 6, line 34, teaches that "TF-2 significantly suppressed Cox-2 gene expression in Caco-2 cells. Effects were seen at doses of 50 to 100 μM TF-2 [i.e, theaflavin-3-gallate and theaflavin-3'-gallate mixture] . . . effects of TF-2 were Cox-2-specific." The Examiner has not established that TF-2 in an effective amount is necessarily present in the preparations taught by DE19627344.

4. To the extent DE19627344 teaches method of treating cancer by administering a composition comprising theaflavins, Applicant respectfully submits that treating cancer by administering a composition having theaflavins is not sufficient for DE19627344 to anticipate the instant claims since that teaching does not necessarily mean suppressing Cox-2 gene expression by using an effective amount of TF2. Further, as the Examiner acknowledged on page 15 of the Office Action, that cancer [treatment] "does not necessarily have to be associated with [suppression of] Cox-2 gene expression."

Therefore, the claim limitations "suppressing Cox-2 gene expression" and "theaflavin-3-gallate and theaflavin-3'-gallate mixture . . . in an effective amount to suppress the Cox-2 gene expression" are not inherent to the method of administering the composition taught by DE19627344 and are not met.

As such, given the strict identity required of the test for novelty, the Examiner has not

established a *prima facie* case of anticipation in support of the rejection of claims 6-8, 12-14, 30-32 and 34-36 based on the DE19627344 reference. Therefore, contrary to the Examiner's assertion, DE19627344 does not anticipate claims 6-8, 12-14, 30-32 and 34-36 as it does not teach or disclose each and every limitation in each of these claims.

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §102 are respectfully requested.

IV. Response to Rejections Under 35 U.S.C. §103

Yang, Okuda and Xu

Claims 6-8 and 12-15 stood rejected under 35 U.S.C. §103(a) as obvious over Yang et al. (U) in view of Okuda et al (JP60025933) ("Okuda")and Xu et al. European J. of Cancer Prevention (1993). Vol. 2: 327-335 ("Xu"). Applicant respectfully traverses this rejection.

Yang is discussed above. Yang does not disclose or suggest Cox-2 suppression by theaflavins. Yang does not disclose or suggest Cox-2 suppression by using an effective amount of theaflavin-3-gallate and theaflavin-3'-gallate mixture or how this can be done. Okuda and Xu do not cure the deficiencies in Yang.

Even if the teachings of Yang, Okuda and Xu are combined, one cannot arrive at the claimed invention because the combination does not suggest anything about suppressing Cox-2 gene expression or about the use of theaflavin-3-gallate and theaflavin-3'-gallate mixture in an effective amount to suppress the Cox-2 gene expression.

To the extent the prior art provides any suggestion for adjusting the amount of a given theaflavin in a composition, it would be for theaflavin-3, 3'-digallate (also known as TF3) or green tea components. Recently, for example, Liang et al., (1999), Carcinogenesis 20:733-736, compared the effectiveness of TF1, TF2 and TF3 for the inhibition of carcinogenesis. They state on page 736 that "[t]he present studies clearly demonstrate that TF-3 may be the major active component that contributes to the antiproliferative activity in black tea. Moreover, TF-3 appears to be a better inhibitor of tyrosine receptor kinase than green tea polyphenol EGCG." DE19627344 states on page 8, lines 1-3 that "[t]he preparations examined are made primarily from green tea, since they possess large amounts of components of relevance here

(polyphenols)." See also, Chen et al., 1998, Cancer Letters, 129:173-179, which reference is of record, and the Yang et al., reference disclosing a 17.5% EGCG at page 196 as further evidence of teachings or suggestions provided by the prior art. Given these explicit prior art teachings, where is the suggestion to use a composition containing a sufficient amount of theaflavin-3-gallate and theaflavin-3'-gallate to treat cancer?

While it may be argued, in light of Yang, that it would have been obvious to one skilled in the art to try [1] the claimed method, it would nevertheless be nonobvious to one of ordinary skill in the art because the differential effects of TF-2 was unexpected. Such an unexpected result, which is of a significant practical advantage, is an indication of nonobviousness. *In re Soni,* 34 USPQ2d 1684 (Fed. Cir. 1995).

In view of the foregoing, Applicant respectfully submits that the Examiner has not established a *prima facie* case of obviousness of claims 6-9 and 12-15 based on the combination of Yang, Okuda and Xu under 35 U.S.C. § 103(a). Even if *prima facie* obviousness has been established, which it has not, it is urged that the cited art nonetheless fails to render the present invention obvious under a proper § 103 analysis.

DE19627344, Okuda and Xu

Claims 6-8, 12-14, 30-32 and 34-36 stood rejected under 35 U.S.C. §103(a) as obvious over DE19627344 in view of Okuda et al (JP60025933) ("Okuda")and Xu et al. European J. of Cancer Prevention (1993). Vol. 2: 327-335 ("Xu"). Applicant respectfully traverses this rejection.

DE19627344 is discussed above. DE19627344 does not disclose or suggest Cox-2 suppression by theaflavins. DE19627344 does not disclose or suggest Cox-2 suppression by using an effective amount of theaflavin-3-gallate and theaflavin-3'-gallate mixture to suppress Cox-2 gene expression or how this can be done. Okuda and Xu do not cure the deficiencies in DE19627344.

Even if the teachings of DE19627344, Okuda and Xu are combined, one cannot arrive at

---

[1] Obvious to try is an improper ground for a §103 rejection. *In re Dow Chemical Co.* 5 USPQ2d 1529 (Fed Cir 1988).

the claimed invention because the combination does not suggest anything about suppressing Cox-2 gene expression or about the use of theaflavin-3-gallate and theaflavin-3'-gallate mixture in an effective amount to suppress the Cox-2 gene expression.

To the extent the prior art provides any suggestion for adjusting the amount of a given theaflavin in a composition, it would be for theaflavin-3, 3'-digallate (also known as TF3) or green tea components. Recently, for example, Liang et al., (1999), Carcinogenesis 20:733-736, compared the effectiveness of TF1, TF2 and TF3 for the inhibition of carcinogenesis. They state on page 736 that "[t]he present studies clearly demonstrate that TF-3 may be the major active component that contributes to the antiproliferative activity in black tea. Moreover, TF-3 appears to be a better inhibitor of tyrosine receptor kinase than green tea polyphenol EGCG." DE19627344 states on page 8, lines 1-3 that "[t]he preparations examined are made primarily from green tea, since they possess large amounts of components of relevance here (polyphenols)." See also, Chen et al., 1998, Cancer Letters, 129:173-179, which reference is of record, and the Yang et al., reference disclosing a 17.5% EGCG at page 196 as further evidence of teachings or suggestions provided by the prior art. Given these explicit prior art teachings, where is the motivation to use a composition containing a sufficient amount of theaflavin-3-gallate and theaflavin-3'-gallate to treat cancer?

While it may be argued, in light of DE19627344, that it would have been obvious to one skilled in the art to try the claimed method, it would nevertheless be nonobvious to one of ordinary skill in the art because the differential effects of TF-2 was unexpected. Such an unexpected result, which is of a significant practical advantage, is an indication of nonobviousness. *In re Soni,* 34 USPQ2d 1684 (Fed. Cir. 1995).

In view of the foregoing, Applicant respectfully submits that the Examiner has not established a *prima facie* case of obviousness of claims 6-8, 12-14, 30-32 and 34-36 based on the combination of DE19627344, Okuda and Xu under 35 U.S.C. § 103(a). Even if *prima facie* obviousness has been established, which it has not, it is urged that the cited art nonetheless fails to render the present invention obvious under a proper § 103 analysis.

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. §103 (a) are respectfully requested.

V. Conclusion

Applicant believes this response to be a full and complete response to the Office Action. Accordingly, favorable reconsideration in view of this response and allowance of all of the pending claims are earnestly solicited.

Respectfully submitted,

January 14, 2005

Nanda P.B.A. Kumar
Registration No. 44,853
William J. McNichol, Jr.
Registration No. 31,179
Attorneys for Applicant

REED SMITH LLP
2500 One Liberty Place, 1650 Market Street
Philadelphia, Pennsylvania 19103-7301
Fax: (215) 851-1420
William J. McNichol, Jr., Esq.
(215-241-7950)
Nanda P.B.A. Kumar, Esq.
(215-241-7991)